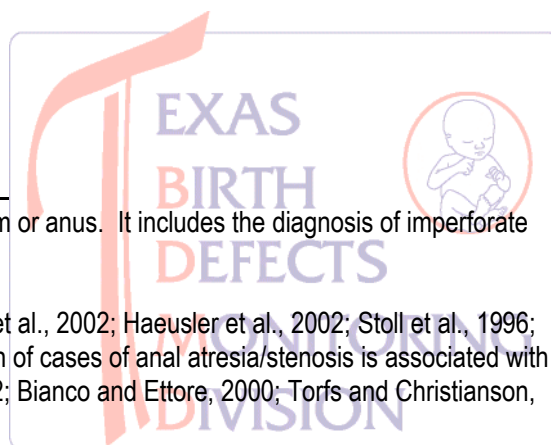


BIRTH DEFECT RISK FACTOR SERIES: ANAL ATRESIA/STENOSIS

DEFINITION

Anal atresia/stenosis is the absence, closure, or constriction of the rectum or anus. It includes the diagnosis of imperforate anus. Anal atresia/stenosis is usually diagnosed shortly after delivery.

Anal atresia/stenosis is often associated with other birth defects (Garne et al., 2002; Haeusler et al., 2002; Stoll et al., 1996; Harris et al., 1995; Castilla and Lopez-Camelo, 1990). A small proportion of cases of anal atresia/stenosis is associated with chromosomal abnormalities, particularly trisomy 21 (Haeusler et al., 2002; Bianco and Ettore, 2000; Torfs and Christianson, 1998; Stoll et al., 1997; Kallen et al., 1996; Harris et al., 1995).



DEMOGRAPHIC AND REPRODUCTIVE FACTORS

No significant association between **race/ethnicity** and anal atresia/stenosis has been identified (Stoll et al., 1997; Yang et al., 1994), although several studies have reported the anal atresia/stenosis rate to be slightly lower in African-Americans (Harris et al., 1995; Chavez et al., 1988), and another reported the rate of rectal/anal atresia to be higher in Europeans and South Asians than in Caribbeans (Leck and Lancashire, 1995).

One investigation found no **secular trend** for anal atresia/stenosis (Spouge and Baird, 1986), while another investigation reported an increase in the rate of the defects over time (Yang et al., 1994). Anal atresia/stenosis does not appear to demonstrate **seasonal variation** (Stoll et al., 1997; Castilla et al., 1990).

Geographic location does not affect risk for anal atresia/stenosis (Stoll et al., 1997), except that one investigation identified an increased risk of the defects with higher **altitude** (Castilla et al., 1999).

The association between anal atresia/stenosis and **maternal age** has been reported to be U-shaped (Harris et al., 1995; Yang et al., 1994) or to increase with increasing maternal age (Myers et al., 2001), although another study found no association between maternal age and the condition (Stoll et al., 1997). **Paternal age** does not appear to influence anal atresia/stenosis risk (Stoll et al., 1997; McIntosh et al., 1995).

Infant sex may influence anal atresia/stenosis risk, with the condition being more common among males (Haeusler et al., 2002; Lary and Paulozzi, 2001; Myers et al., 2001; Cuschieri and EUROCAT Working Group, 2001; Riley et al., 1998; Harris et al., 1995; Spouge and Baird, 1986), although several studies found no relationship between sex and anal atresia/stenosis (Stoll et al., 1997; Yang et al., 1994).

Anal atresia/stenosis risk increases with lower **birth weight** (Riley et al., 1998; Stoll et al., 1997; Mili et al., 1991) but is not associated with large for gestational age (Lapunzina et al., 2002). Anal atresia/stenosis risk is elevated with **prematurity** (Rasmussen et al., 2001). Large intestinal atresia has been associated with **intrauterine growth retardation** (Khoury et al., 1988). Various investigations found a decrease in risk of these defects with increasing **parity** and an increase in risk with **multiple gestation pregnancy** (Mastroiacovo et al., 1999; Riley et al., 1998; Harris et al., 1995; Doyle et al., 1991; Kallen et al., 1986); however, a different investigation reported no such associations (Stoll et al., 1997).

One study identified higher risk of anal atresia/stenosis with **consanguinity** (Stoll et al., 1997) while another study found no association (Rittler et al., 2001). A small percentage of cases with anal atresia/stenosis have a **family history** of the same defect (Stoll et al., 1997; Spouge and Baird, 1986).

FACTORS IN LIFESTYLE OR ENVIRONMENT

Maternal education does not appear to affect risk for anal atresia/stenosis (Stoll et al., 1997). One investigation identified no significant association between **maternal nursing occupation** and risk of atresia/stenosis of the colon, rectum, or anus (Matte et al., 1993). **Paternal occupations of printing or sales** do not appear to increase risk of rectal atresia (Irgens et al., 2000). A review article noted increased risk of anal atresia/stenosis with paternal occupation of **vehicle manufacturer** (Chia and Shi, 2002).

Maternal diabetes may increase risk for anal atresia/stenosis (Aberg et al., 2001; Bianchi et al., 2000; Stoll et al., 1997; Becerra et al., 1990), although one investigation reported no association between imperforate anus and diabetes (Ramos-Arroyo et al., 1992). There is no apparent association between anal atresia/stenosis and **maternal epilepsy, hypertension, fever, flu, hypothyroidism, or hyperthyroidism** (Stoll et al., 1997; Khoury et al., 1989).

Anal atresia/stenosis has been reported in infants whose mothers took **thalidomide** during pregnancy (Bianchi et al., 2000). One study observed no association between maternal use of the antibiotic **oxytetracycline** during pregnancy and rectal-anal atresia/stenosis (Czeizel and Rockenbauer, 2000), and others found no relationship between **cephalosporin antibiotics, nalidixic acid, ampicillin**, or the **benzodiazepines** nitrazepam, medazepam, tofisopam, alprazolam, and clonazepam and recto-anal atresia or stenosis (Eros et al., 2002; Czeizel et al., 2001a; Czeizel et al., 2001b; Czeizel et al., 2001c). Investigations into the association between **alcohol** and anal atresia/stenosis are mixed (Bianchi et al., 2000; Stoll et al., 1997). Maternal **smoking** and exposure to **X-rays** do not appear to cause anal atresia/stenosis (Honein et al., 2001; Stoll et al., 1997; Yuan et al., 1995; Van Den Eeden et al., 1990; Shiono, 1986), although one investigation observed increased risk of atresia of rectum, anal canal, large intestine with maternal smoking (Cornel et al., 1996).

Living in proximity to **hazardous waste sites** has not been found to affect risk of anal atresia (Dolk et al., 1998). An investigation failed to identify any significant association between anal atresia and proximity to various types of **industry** (Castilla et al., 2000). Anal atresia does not appear to be related to **water chlorination** (Kallen and Robert, 2000). One study reported no increased risk of skin-covered anus in regions of Belarus contaminated after the **Chernobyl** accident (Feshchenko et al., 2002).

No association between maternal **folic acid** use and anal atresia has been reported by one study (Czeizel et al., 1996), while another more recent investigation identified reduced risk of imperforate anus with maternal use of folic acid (Myers et al., 2001). Furthermore, a study that examined **co-trimoxazole**, a combination of trimethoprim and sulfamethoxazole that is a folic acid antagonist, failed to find any association between the medication and anal-rectal atresia/stenosis (Czeizel, 1990).

PREVALENCE

The reported prevalence for anal atresia/stenosis has shown variation between studies, ranging between 1.4 and 5.8 per 10,000 births (Table 1). Differences in prevalence may be due to differences in case inclusion criteria.

Table 1. Prevalence per 10,000 births of anal atresia/stenosis			
Reference	Location	Time period	Rate
Haeusler et al., 2002	Europe	1996-1998	1.4
Garne et al., 2002	Denmark	1980-1993	3.8
Sekhobo and Druschel, 2002	New York, USA	1996	3.3
Cuschieri and EUROCAT Working Group, 2001	Europe	1980-1994	4.3
Rily et al., 1998	Australia	1983-1995	4.0
Stoll et al., 1997	France	1979-1995	4.8

Table 1. Prevalence per 10,000 births of anal atresia/stenosis

Reference	Location	Time period	Rate
Stoll et al., 1996	France	1979-1987	5.2
Harris et al., 1995	France	1976-1990	2.9
Harris et al., 1995	Sweden	1973-1990	3.5
Harris et al., 1995	California, USA	1983-1990	3.6
Stoll and EUROCAT Working Group, 1995	Europe	1980-1990	3.4
Finley et al., 1994	Sweden	1985-1986	5.8
Finley et al., 1994	Alabama, USA	1986-1987	2.5
Yang et al., 1994	Maryland, DC, Virginia, USA	1980-1987	3.0
Castilla and Lopez-Camelo, 1990	Central & South America	1982-1986	3.7
Calzolari et al., 1987	Italy	1978-1984	3.2
Spouge and Baird, 1986	Canada	1964-1982	4.0
Czeizel and Vitez, 1981	Hungary	1970-1977	1.8

REFERENCES

Aberg A, Westbom L, Kallen B. Congenital malformations among infants whose mothers had gestational diabetes or preexisting diabetes. *Early Hum Dev* 2001;61:85-95.

Becerra JE, Khoury MJ, Cordero JF, Erickson JD. Diabetes mellitus during pregnancy and the risks for specific birth defects: a population-based case-control study. *Pediatrics* 1990;85:1-9.

Bianchi DW, Crombleholme TM, D'Alton ME. Anorectal atresia (imperforate anus). In: *Fetology: Diagnosis and Management of the Fetal Patient*. New York: McGraw-Hill, 2000; pp. 499-505.

Bianco S, Ettore G. Anorectal malformations and Down's syndrome. *Paediatr Perinat Epidemiol* 2000;14:372.

Calzolari E, Cavazzuti GB, Cocchi G, Contrino C, Magnani C, Moretti M, Roncarati E, Salvioli GP, Volpato S. Congenital malformations in 100,000 consecutive births in Emilia Romagna region, northern Italy: comparison with the EUROCAT data. *Eur J Epidemiol* 1987;3:423-430.

Castilla EE, Campana H, Camelo JS. Economic activity and congenital anomalies: an ecologic study in Argentina. *Environ Health Perspect* 2000;108:193-197.

Castilla EE, Lopez-Camelo JS, Campana H. Altitude as a risk factor for congenital anomalies. *Am J Med Genet* 1999;86:9-14.

Castilla EE, Lopez-Camelo JS. The surveillance of birth defects in South America: I. The search for time clusters: epidemics. In: *Advances in Mutagenesis Research*. Springer-Verlag, New York. 1990 pp. 191-210.

Castilla EE, Orioli IM, Lugarinho R, Dutra GP, Lopez-Camelo JS, Campana HE, Spagnolo A, Mastroiacovo P. Monthly and seasonal variations in the frequency of congenital anomalies. *Int J Epidemiol* 1990;19:399-404.

Chavez GF, Cordero JF, Becerra JE. Leading major congenital malformations among minority groups in the United States, 1981-1986. *Mor Mortal Wkly Rep CDC Surveill Summ* 1988;37:17-24.

Chia SE, Shi LM. Review of recent epidemiological studies on paternal occupations and birth defects. *Occup Environ Med*. 2002;59:149-155.

Cornel MC, Erickson JD, Khoury MJ, James LM, Liu Y. Population-based birth-defect and risk factor surveillance: data from the Northern Netherlands. *Int J Risk Safety Med* 1996;8:197-209.

Cuschieri A, EUROCAT Working Group. Descriptive epidemiology of isolated anal anomalies: a survey of 4.6 million births in Europe. *Am J Med Genet* 2001;103:207-215.

Czeizel A, Vitez M. Birth prevalence of five congenital abnormalities of medium frequency in Budapest. *Acta Paediatr Acad Sci Hung* 1981;22:299-308.

Czeizel A. A case-control analysis of the teratogenic effects of cotrimoxazole. *Reprod Toxicol* 1990;4:305-313.

Czeizel AE, Toth M, Rockenbauer M. Population-based case control study of folic acid supplementation during pregnancy. *Teratology* 1996;53:345-351.

Czeizel AE, Rockenbauer M. A population-based case-control teratologic study of oral oxytetracycline treatment during

- pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2000;88:27-33.
- Czeizel AE, Rockenbauer M, Sorensen HT, Olsen J. Use of cephalosporins during pregnancy and in the presence of congenital abnormalities: a population-based, case-control study. *Am J Obstet Gynecol* 2001a;184:1289-1296.
- Czeizel AE, Sorensen HT, Rockenbauer M, Olsen J. A population-based case-control teratologic study of nalidixic acid. *Int J Gynaecol Obstet* 2001b;73:221-228.
- Czeizel AE, Rockenbauer M, Sorensen HT, Olsen J. A population-based case-control teratologic study of ampicillin treatment during pregnancy. *Am J Obstet Gynecol* 2001c;185:140-147.
- Dolk H, Vrijheid M, Armstrong B, Abramsky L, Bianchi F, Garne E, Nelen V, Robert E, Scott JE, Stone D, Tenconi R. Risk of congenital anomalies near hazardous-waste landfill sites in Europe: the EUROHAZCON study. *Lancet* 1998;352:423-427.
- Doyle PE, Beral V, Botting B, Wale CJ. Congenital malformations in twins in England and Wales. *J Epidemiol Community Health* 1991;45:43-48.
- Eros E, Czeizel AE, Rockenbauer M, Sorensen HT, Olsen J. A population-based case-control teratologic study of nitrazepam, medazepam, tofisopam, alprazolam and clonazepam treatment during pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2002;101:147-154.
- Feshchenko SP, Schroder HC, Muller WE, Lazjuk GI. Congenital malformations among newborns and developmental abnormalities among human embryos in Belarus after Chernobyl accident. *Cell Mol Biol* 2002;48:423-426.
- Finley WH, Gustavson KH, Hall TM, Hurst DC, Barganier CM, Wiedmeyer JA. Birth defects surveillance: Jefferson County, Alabama, and Uppsala County, Sweden. *South Med J* 1994;87:440-445.
- Harris J, Kallen B, Robert E. Descriptive epidemiology of alimentary tract atresia. *Teratology* 1995;52:15-29.
- Garne E, Rasmussen L, Husby S. Gastrointestinal malformations in Funen County, Denmark - epidemiology, associated malformations, surgery and mortality. *Eur J Pediatr Surg* 2002;12:101-106.
- Haeusler MC, Berghold A, Stoll C, Barisic I, Clementi M. Prenatal ultrasonographic detection of gastrointestinal obstruction: results from 18 European congenital anomaly registries. *Prenat Diagn* 2002;22:616-623.
- Honein MA, Paulozzi LJ, Watkins ML. Maternal smoking and birth defects: validity of birth certificate data for effect estimation. *Public Health Rep* 2001;116:327-335.
- Irgens A, Kruger K, Skorge AH, Irgens LM. Birth defects and paternal occupational exposure. Hypotheses tested in a record linkage based dataset. *Acta Obstet Gynecol Scand* 2000;79:465-470.
- Kallen B, Mastroiacovo P, Robert E. Major congenital malformations in Down syndrome. *Am J Med Genet* 1996;65:160-166.
- Kallen BA, Robert E. Drinking water chlorination and delivery outcome-a registry-based study in Sweden. *Reprod Toxicol* 2000;14:303-309.
- Khoury MJ, Becerra JE, d'Almada PJ. Maternal thyroid disease and risk of birth defects in offspring: a population-based case-control study. *Paediatr Perinat Epidemiol* 1989;3:402-420.
- Khoury MJ, Erickson JD, Cordero JF, McCarthy BJ. Congenital malformations and intrauterine growth retardation: a population study. *Pediatrics* 1988;82:83-90.
- Lapunzina P, Lopez Camelo JS, Rittler M, Castilla EE. Risks of congenital anomalies in large for gestational age infants. *J Pediatr* 2002;140:200-204.
- Lary JM, Paulozzi LJ. Sex differences in the prevalence of human birth defects: a population-based study. *Teratology* 2001;64:237-251.
- Leck I, Lancashire RJ. Birth prevalence of malformations in members of different ethnic groups and in the offspring of matings between them, in Birmingham, England. *J Epidemiol Community Health* 1995;49:171-179.
- Mastroiacovo P, Castilla EE, Arpino C, Botting B, Cocchi G, Goujard J, Marinacci C, Merlob P, Metneki J, Mutchinick O, Ritvanen A, Rosano A. Congenital malformations in twins: an international study. *Am J Med Genet* 1999;83:117-124.
- Matte TD, Mulinare J, Erickson JD. Case-control study of congenital defects and parental employment in health care. *Am J Ind Med* 1993;24:11-23.
- McIntosh GC, Olshan AF, Baird PA. Paternal age and the risk of birth defects in offspring. *Epidemiology* 1995;6:282-288.
- Mili F, Edmonds LD, Khoury MJ, McClearn AB. Prevalence of birth defects among low-birth-weight infants. A population study. *Am J Dis Child* 1991;145:1313-1318.
- Myers MF, Li S, Correa-Villasenor A, Li Z, Moore CA, Hong SX, Berry RJ. Folic acid supplementation and risk for imperforate anus in China. *Am J Epidemiol* 2001;154:1051-1056.
- Ramos-Arroyo MA, Rodriguez-Pinilla E, Cordero JF. Maternal diabetes: the risk for specific birth defects. *Eur J Epidemiol* 1992;8:503-508.
- Rasmussen SA, Moore CA, Paulozzi LJ, Rhodeniser EP. Risk for birth defects among premature infants: A population-based study. *J Pediatr* 2001;138:668-673.
- Riley MM, Halliday JL, Lumley JM. Congenital malformations in Victoria, Australia, 1983-95: an overview of infant characteristics. *J Paediatr Child Health* 1998;34:233-240.
- Rittler M, Liascovich R, Lopez-Camelo J, Castilla EE. Parental consanguinity in specific types of congenital anomalies. *Am J Med Genet* 2001;102:36-43.
- Sekhobo JP, Druschel CM. An evaluation of congenital malformations surveillance in New York State: an application of Centers for Disease Control and Prevention (CDC) guidelines for

evaluating surveillance systems. Public Health Rep 2001;116:296-305.

Shiono PH, Klebanoff MA, Berendes HW. Congenital malformations and maternal smoking during pregnancy. Teratology 1986;34:65-71.

Spouge D, Baird PA. Imperforate anus in 700,000 consecutive liveborn infants. Am J Med Genet Suppl 1986;2:151-161.

Stoll C, Alembik Y, Roth MP, Dott B. Risk factors in congenital anal atresias. Ann Genet 1997;40:197-204.

Stoll C, Alembik Y, Dott B, Roth MP. Evaluation of prenatal diagnosis of congenital gastro-intestinal atresias. Eur J Epidemiol 1996;12:611-616.

Stoll C, EUROCAT Working Group. Distribution of single organ malformations in European populations. Ann Genet 1995;38:32-

43.

Torfs CP, Christianson RE. Anomalies in Down syndrome individuals in a large population-based registry. Am J Med Genet 1998;77:431-438.

Van Den Eeden SK, Karagas MR, Daling JR, Vaughan TL. A case-control study of maternal smoking and congenital malformations. Paediatr Perinat Epidemiol 1990;4:147-155.

Yang P, Khoury MJ, Stewart WF, Beaty TH, Chee E, Beatty JC, Diamond EL, Gordis L. Comparative epidemiology of selected midline congenital abnormalities. Genet Epidemiol 1994;11:141-154.

Yuan P, Okazaki I, Kuroki Y. Anal atresia: effect of smoking and drinking habits during pregnancy. Jpn J Hum Genet 1995;40:327-332.

Please Note: The primary purpose of this report is to provide background necessary for conducting cluster investigations. It summarizes literature about risk factors associated with this defect. The strengths and limitations of each reference were not critically examined prior to inclusion in this report. Consumers and professionals using this information are advised to consult the references given for more in-depth information.

This report is for information purposes only and is not intended to diagnose, cure, mitigate, treat, or prevent disease or other conditions and is not intended to provide a determination or assessment of the state of health. Individuals affected by this condition should consult their physician and when appropriate, seek genetic counseling
